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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/566,588	03/09/2006	Taro Yoshikawa	126835	7199

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EXAMINER	
LAU, JONATHAN S	

ART UNIT	PAPER NUMBER
1623	

NOTIFICATION DATE	DELIVERY MODE
03/31/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/566,588	YOSHIKAWA ET AL.	
	Examiner	Art Unit	
	Jonathan S. Lau	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 January 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4 and 9-14* is/are pending in the application.

4a) Of the above claim(s) *11-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 4, 9 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is responsive to Applicant's Amendment and Remarks, filed 4 Jan 2010, in which claim 9 is amended to change the scope and breadth of the claim.

This application is the national stage entry of PCT/JP04/11462, filed 10 Aug 2004; and claims benefit of foreign priority document JAPAN 2003-292135, filed 12 Aug 2003; currently an English language translation of this foreign priority document has not been filed.

Claims 1, 3, 4 and 9-14 are pending in the current application. Claims 11-14, drawn to non-elected inventions, are withdrawn. Claims 1, 3, 4, 9 and 10 are examined on the merits herein.

Rejections Withdrawn

Applicant's Amendment, filed 4 Jan 2010, with respect to claim 9 rejected under 35 U.S.C. 112, second paragraph, as being indefinite has been fully considered and is persuasive, as amended claim 9 recites the concentration is more than 70% of an initial concentration of cysteine in said composition.

This rejection has been **withdrawn**.

The following modified grounds of rejection are necessitated by Applicant's Amendment, filed 4 Jan 2010, in which claim 9 is amended to change the scope and breadth of the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Amended Claims 1, 3, 4, 9 and 10 and rejected under 35 U.S.C. 103(a) as being unpatentable over Van Rossum et al. (Aliment. Pharmacol. Ther. 1998, 12, p199-205, cited in PTO-892) in view of Chen et al. (US Patent Application Publication 2002/0147201, published 10 Oct 2002, cited in PTO-892).

Van Rossum et al. teaches glycyrrhizin having anti-viral and hepatoprotective effects (abstract) in the form of Stronger Neo Minophagen C, a solution for intravenous

use comprising of 2 mg/mL glycyrrhizin, 1 mg/mL cysteine, and 20 mg/mL glycine in physiological saline (page 203, left column, paragraph 1 in section Clinical Investigations), specifically noting the required elements of glycyrrhizin, glycine and cysteine. Van Rossum et al. teaches the composition administered at a dose of 80 mg glycyrrhizin daily (page 203, left column, paragraph 1 in section Clinical Investigations). Applicant provides evidence that Stronger Neo Minophagen C contains glycyrrhizin as monoammonium glycyrrhizin and cysteine as L-cysteine hydrochloride, and that Stronger Neo Minophagen C further comprises sodium sulfite (NPL citation 7 at IDS mailed 06 Jun 2006).

Van Rossum et al. does not specifically teach said injectable composition containing 8 to 16 mg/mL glycyrrhizin , 3 to 6 mg/mL cysteine, and 80 to 160 mg/mL glycine wherein substantially no sulfite is contained in the composition (instant claim 1). Van Rossum et al. does not specifically teach said injectable composition containing 8 to 16 mg/mL monoammonium glycyrrhizin, 4 to 8 mg/mL cysteine hydrochloride, and 80 to 160 mg/mL glycine wherein substantially no sulfite is contained (instant claim 9).

Chen et al. teaches water soluble complexes comprising glycyrrhizin and an active agent (page 2, paragraph 19) including antiviral agents (page 2, paragraph 20). Chen et al. teaches said composition as a liquid for parenteral administration, or for injection, also containing pharmaceutical excipients (page 3, paragraph 21). Chen et al. teaches preservatives such as sodium benzoate, sorbic acid, propionic acid, acetic acid, nitride and nitrates are known in the art as equivalent preservatives as sulfites within the art of the pharmaceutical compositions comprising glycyrrhizin taught by Chen et al.

(page 6, paragraph 59). Chen et al. teaches said compositions containing glycyrrhizin soluble at an aqueous concentration of approximately 12.3 mg/mL (822.9 g/mol * 0.015 M) (figure 2 at drawing sheet 2 and page 9, paragraph 94) and 8.2 mg/mL (822.9 g/mol * 0.010 M) and 16.4 mg/mL (822.9 g/mol * 0.020 M) (figure 4 at drawing sheet 4).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine Van Rossum et al. in view of Chen et al. Both Van Rossum et al. and Chen et al. are drawn to injectable compositions containing glycyrrhizin having anti-viral activity. One of skill in the art would be motivated to increase the amount of glycyrrhizin, glycine and cysteine because Van Rossum et al. teaches the composition administered at a dose of 80 mg glycyrrhizin daily. One of skill in the art would be motivated to select a concentration of 8.2 mg/mL or 12.3 mg/mL because Chen et al. teaches water soluble complexes comprising that concentration of glycyrrhizin . One of ordinary skill in the art would be motivated to increase the concentration of glycine and cysteine proportionately with the glycyrrhizin because Van Rossum et al. teaches glycine and cysteine play a physiological role. One of skill in the art would have a reasonable expectation of success to increase the concentration of glycine and cysteine proportionately with the glycyrrhizin because it is well known in the art that the amino acids glycine and cysteine are very soluble in water. It would have been *prima facie* obvious to substitute sodium sulfite for another preservative to give a composition wherein substantially no sulfite is contained because Chen et al. teaches preservatives such as sodium benzoate, sorbic acid, propionic acid, acetic acid, nitride and nitrates are known in the art as equivalent preservatives as sulfites. An express suggestion to

substitute one equivalent component or process for another is not necessary to render such substitution obvious, see MPEP 2144.06 II.

The property of the state of the composition after it is stored at 60 °C for 14 days (instant claim 9) is deemed to be an inherent property of the composition, and therefore necessarily present in the composition taught by Van Rossum et al. in view of Chen et al. See MPEP 2112.01 II, "Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present.

Response to Applicant's Remarks:

Applicant's remarks, filed 4 Jan 2010, have been fully considered and not found to be persuasive.

Applicant notes that Chen is drawn to a glycyrrhizin complexed with an active agent, not glycyrrhizin as a pharmaceutical agent in its own right. However, the rejection is made over Van Rossum et al. in view of Chen, not Chen alone. Van Rossum teaches glycyrrhizin having pharmaceutical activity (abstract) and at page 203, left column, paragraph 4 teaches the combination of glycyrrhizin with cysteine and glycine, where cysteine and glycine are taught to have pharmaceutical activity of their own. Therefore the composition made obvious over Van Rossum et al. in view of Chen is drawn to glycyrrhizin complexed with active agents cysteine and glycine combined with the teaching of Van Rossum of glycyrrhizin having pharmaceutical activity.

Applicant notes that Chen discloses both sulfites and other preservatives as acceptable preservatives. However, Chen does not require the invention made obvious over Van Rossum et al. in view of Chen to include sulfites. The instant application discloses that when sodium sulfite is not used as a stabilizer the stability of the instant composition in high concentrations are improved (specification, page 3). As provided by MPEP 2141.02 III.:

> "[A] patentable invention may lie in the discovery of the source of a problem even though the remedy may be obvious once the source of the problem is identified. This is part of the 'subject matter as a whole' which should always be considered in determining the obviousness of an invention under 35 U.S.C. § 103." *In re Sponnoble*, 405 F.2d 578, 585, 160 USPQ 237, 243 (CCPA 1969). However, "discovery of the cause of a problem . . does not always result in a patentable invention. . . . [A] different situation exists where the solution is obvious from prior art which contains the same solution for a similar problem." *In re Wiseman*, 596 F.2d 1019, 1022, 201 USPQ 658, 661 (CCPA 1979) (emphasis in original).

Applicant notes that Chen does not provide reason or rationale to alter the SNMC of Van Rossum that excludes sulfites. However, Mollica et al. (Journal of Pharmaceutical Sciences, 1978, 67(4), p443-465, of record), cited as evidence of the level of ordinary skill in the art of pharmaceutical formulations, teaches the stability of pharmaceuticals is an implicit motivation to one of ordinary skill in the art of pharmaceutical formulations, and provides evidence that it is known that the choice of excipients, such as sulfites, affects the stability. Therefore, in view of the level of ordinary skill of one in the art of pharmaceutical formulations, the reason or rationale to alter the SNMC of Van Rossum lies in the implicit motivation to formulate stable pharmaceuticals and even if applicants discovered the cause of a problem, the solution would have been obvious from the prior

art which contained the same solution for a similar problem, choosing excipients to formulate stable pharmaceuticals.

Conclusion

No claim is found to be allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is 571-270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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